

REMARKS

Reconsideration of the Final Office Action mailed October 15, 2003, (hereinafter "instant Office Action"), entry of the foregoing amendments and withdrawal of the rejection of claims 1-40 and 44-88, are respectfully requested.

In the instant Office Action, claims 1-40 and 44-88 are listed as pending, and claims 1-40 and 44-88 are listed as rejected.

The Examiner has rejected claims 1-40 and 44-88 under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse this rejection. Applicants' response to the Examiner's enumerated points are numbered accordingly to track the Examiner's points.

ii) With respect to the term "substituted", Applicants maintain the arguments presented in the Replies filed August 26, 2002, November 26, 2002 and July 26, 2003. However, without conceding to the correctness of the Examiner's rejections and for the sole purpose of expediting prosecution of the instant application and to place it in condition for allowance, Applicants have amended Claim 1 to list suitable substituents for R_a, R_b, R_c, Z¹⁰¹, Z¹⁰², Z²⁰⁰, R₁, R₃, R_g, A, B and E. Support for these amendments can be found, *inter alia*, on page 55, lines 11-24. Applicants have also amended Claim 1 to correct a typographical error. "R₁" has been amended to read "R_b".

iv) Regarding the term "heterocyclic", Applicants maintain the arguments presented in the Replies filed August 26, 2002, November 26, 2002 and July 26, 2003. Without conceding to the correctness of the Examiner's rejections and for the sole purpose of expediting prosecution of the instant application and to place it in condition for allowance, Applicants have amended Claims 1, 5-14, 16, 18-20, 22, 24, 31, 32, 52, 65 and 67 to list suitable heterocycles. Support for these amendments can be found, *inter alia*, on page 53, line 23 to page 54, line 9.

v) The Examiner alleges that in claims 33 and 34 it is unclear why one would need to inhibit one or more protein kinase activity and that it is unclear who needs such inhibition and what is accomplished. On page 3 of the instant Office Action, the Examiner states that the specification fails to teach any benefit to be gained from such actions. The benefit of inhibiting protein kinase activities *in vitro* is to test for pharmaceuticals or diagnostics as well as to initially

estimate therapeutic dosages. Inhibiting protein kinase activities in mammals with below normal protein kinase activities or asymptomatic mammals with upregulated protein kinase activities would be beneficial because such inhibition would regulate and modulate abnormal or inappropriate cell proliferation, differentiation or metabolism, as stated on page 23, lines 27-30 of the instant specification.

In the Office Action mailed February 26, 2003, the Examiner also rejected claims 1-88 under 35 U.S.C. §112, second paragraph, with respect to the term "prodrugs". Since the Examiner has not raised this issue again in the instant office action, Applicants believe that this rejection has been overcome by the amendments made in the Reply mailed July 28, 2003. In the event that Applicants' belief is incorrect, Applicants respectfully request that the Examiner address this in the next Office Action. Based upon the foregoing, the rejections of claims 1-40 and 44-88 under 35 U.S.C. §112, second paragraph, is obviated and should be withdrawn.

The Examiner has rejected claims 33-51 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification to enable one to make or use the invention. Applicants respectfully traverse this rejection. Regarding the claims drawn to the treatment of solid tumors and affecting angiogenesis, without conceding to the correctness of the Examiner's rejections and for the sole purpose of expediting prosecution of the instant application and to place it in condition for allowance, Applicants have amended claim 40 to delete the term "solid tumor". Regarding the term "affecting angiogenesis", without conceding to the correctness of the Examiner's rejections and for the sole purpose of expediting prosecution of the instant application and to place it in condition for allowance, Applicants have cancelled claim 36 without waiver or prejudice to Applicants' right to pursue the cancelled subject matter in a continuation or divisional application.

On page 3 of the instant Office Action, the Examiner states that the specification fails to teach any benefit to be gained from such actions. The benefit of inhibiting protein kinase activities *in vitro* is to test for pharmaceuticals or diagnostics as well as to initially estimate therapeutic dosages. Inhibiting protein kinase activities in mammals with below normal protein kinase activities or asymptomatic mammals with upregulated protein kinase activities would be beneficial because such inhibition would regulate and modulate abnormal or inappropriate cell proliferation, differentiation or metabolism, as stated on page 23, lines 27-30 of the instant specification.

With respect to the Examiner's quotation of Brenner v. Manson, 148 USPQ at 696: "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion", Applicants submit that the Examiner has taken the quotation out of context. Brenner v. Manson concerned an application for a product by process for which no utility was disclosed for the product. This differs from the instant case wherein specific compounds are disclosed as well as numerous practical applications for them, i.e. many diseases and disorders in which the compounds can be used. The instant application is grounded in the world of commerce in that it is directed to therapeutics which can be used to treat diseases. It is not directed to compounds with no known utility. In fact, Applicants list numerous specific diseases and disorders in which the claimed compounds can be utilized.

The Examiner states "As U.S. Court of Customs and Patent Appeals stated In re Diedrich 138 USPQ at 130, quoting with approval from the decision of the board: 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.' Applicants respectfully point out that In re Diedrich concerned a case in which the appellant stated his compounds were "useful for technical and pharmaceutical purposes." Not only did the appellant fail to provide a specific utility for his compounds, but upon appeal the appellant argued that the compounds could be used as X-ray contrast agents and proceeded to cite numerous patents which disclose compounds similar to his as being useful as X-ray contrast agents. The CCPA found that appellant's disclosure failed to satisfy the demands of 35 U.S.C. §112. On the contrary, in the instant case Applicants have provided specific uses for their compounds, i.e. inhibiting protein kinase activity, shown how to measure the inhibition of the protein kinase activity, i.e. providing assays used to test compounds, and listed specific diseases in which the inhibition of protein kinase activity would be beneficial. Applicants have not provided a vague or undefined use for their invention but have instead provided a detailed explanation of how the inhibition of protein kinase activity can be used in a therapeutic context.

Based upon the foregoing, the rejection of claims 33-51 under 35 U.S.C. §112, first paragraph, is obviated and should be withdrawn.

The Examiner has rejected claims 1-40 and 44-88 under 35 U.S.C. §103(a) as allegedly being unpatentable over Altmann et al. (WO 97/49706). Applicants respectfully traverse this rejection. Applicants maintain the arguments presented in the Replies filed August 26, 2002, November 26, 2002 and July 26, 2003.

The Examiner alleges that “the reference teaches a generic group of substituted 7-amino-pyrrolo[3,2-d]pyrimidine derivatives which embraces applicants’ claimed compounds”. The Examiner further states “A claim is unpatentable if only one embodiment within its scope is unpatentable. In re Mraz, 173 USPQ 25, (28 CCPA 1972).” In In re Mraz the claims in question were directed to an apparatus for removing edge burrs from thin metal strips and means of securing them together. The claims at issue in In re Mraz were found to be obvious over the prior art reference cited, as the two references combined to teach all of the elements of the claims in question. However, in the instant office action the Examiner has gone through Altmann et al. and selected certain moieties to compare to the genus disclosed in Claim 1 of the instant application. The Examiner states “Altmann et al. teach R_3 (corresponding to instant R_2) as “cyclo-lower hydrocarbyl”(which is defined on page 2, first line of second paragraph); the prior art R_2 corresponds to hydrogen of the instant claim; the group $-NH_2$ (corresponding to instant $N(R_3)_2$ and the overlap at both the instant and prior art R_1 is seen in the definition of R_1 on pages 1-4 of the reference”. However, Altmann et al. does not disclose a subgenus wherein R_3 is only cyclo-lower hydrocarbyl and R_2 is only hydrogen. Further, the $N(R_3)_2$ group of the instant application is not limited to only $-NH_2$ as the corresponding position is in Altmann et al. The genres disclosed on pages 1, 7, and 8 of Altmann et al. are considerably broader than R_3 as just cyclo-lower hydrocarbyl, R_2 as just hydrogen and the overlapping portions of R_1 . The Examiner has used the benefit of hindsight and gone through Altmann et al. to construct a subgenus that is not present in Altmann et al. to compare to the instant application. Altmann et al. disclose a genus that overlaps with Applicants’ genus. This is not the same fact scenario as was at issue in In re Mraz.

As Applicants have argued in the Replies filed previously, an invention is to be considered as a whole. The claimed invention may not be dissected into discrete elements to be analyzed in isolation, but must be considered as a whole. See, e.g. W.L. Gore & Assoc. Inc. v. Garlock, Inc. 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983)); Jones v. Hardy, 727 f.2d 1524, 1530, 220 USPQ 1021, 1026 (Fed. Cir. 1983). However, the Examiner has dissected the invention into separate elements and analyzed each one individually, when such is not

presented by Applicants, without considering the genus as a whole, by selectively choosing moieties to create a subgenus which is not disclosed in Altmann et al. to compare with the instant application. In determining the differences between the prior art and the claims, the question under 35 U.S.C. §103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. Stratoflex, Inc. v. Aeroquip Corp., 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); Schenck v. Nortron Corp., 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983). The Examiner has not shown how Altmann et al. render obvious the entire genus of Applicants' claim. Applicants maintain that Altmann et al. do not render claims 1-40 and 44-88 obvious. Based upon the foregoing, the rejection of claim 1-40 and 44-88 under 35 U.S.C. §103(a) over Altmann et al. (WO 97/49706) is obviated and should be withdrawn.

No fees are due for the instant amendment since the total number of claims after entry of the amendments hereinabove is not more than the total number of claims that Applicants have paid for to date.

Based upon the foregoing, Applicants believe that claims 1-35, 37-40 and 44-88 are in condition for allowance. Prompt and favorable action is earnestly solicited.

If the Examiner believes that a telephone conference would advance the condition of the instant application for allowance, Applicants invite the Examiner to call Applicants' agent at the number noted below.

Respectfully submitted,

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